Apocrine Hidrocystoma of the Lower Lip: A Case Report and Literature Review

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Abstract The hidrocystomas (HCs) are cystic forms of sweat gland resulting from proliferation of the apocrine secretory coil or eccrine duct. Apocrine -HCs are cystic lesions that arise from the apocrine secretory coil, while eccrine -HCs represent retention cysts of the eccrine duct. The commonest site for such lesions is around the eye, and they may also occur on the ears, scalp, chest, shoulders, or feet. However, HCs of the perioral region are uncommon. The differential diagnosis with minor salivary gland cyst or cystic neoplasms often poses a problem in this site. Here we report a rare case of apocrine -HC of the right lower lip for which excisional biopsy of the lesion was performed. Histopathologically, the lesion was a unilocular cyst lined by a double-layered epithelium of the apocrine secretory type. Immunohistochemically, the secretory epithelium was positive for mammaglobin, gross cystic disease fluid protein 15 (GCDFP-15), cytokeratin 7 (CK 7) and CK18,

and the myoepithelium was positive for alpha-smooth muscle actin (α -SMA) and weakly positive for S100 protein. Here we present this very rare case of apocrine -HC of the lower lip, and discussed regarding differential diagnosis with minor salivary gland cystic lesion in the lip.

Keywords Apocrine hidrocystoma · Lip · Mammaglobin · GCDFP-15 · CK 7 · CK18 · S100 · α -SMA

Introduction

Apocrine hidrocystoma (-HC), also called apocrine cystadenoma, is a benign cystic tumor-like lesion usually presenting as a solitary translucent nodule of cystic consistency [1]. Apocrine -HC arises not from eccrine glands (duct and coil) but from the secretory coil of apocrine sweat glands [1, 2]. Eccrine -HC appears as a retention cyst of the eccrine duct [2]. Histologically, apocrine -HC can be differentiated from eccrine -HC by the presence of secretory cells showing decapitation secretion. Immunohistochemically, apocrine -HC is positive for human milk fat globules, GCDFP-15, CK 7 and α -SMA, whereas eccrine -HC is negative for all of them [3, 4]. Apocrine -HC expresses a secretory-type keratin pattern, whereas eccrine -HC expresses an excretory-type keratin pattern [3]. These lesions are usually located on the face and neck, mainly the periorbital area. However, apocrine -HC developing on the lower lip is very rare, and clinico-pathologically problem point is differential diagnosis between dermal sweat gland lesion and minor salivary gland lesion in this site. Previous reports of apocrine- and eccrine -HCs affecting the lip are listed in Table 1 [3, 5, 6]. In fact, the English literature contains very little information on HCs of the lip [3, 5, 6].

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Table 1 Summary of clinicopathological findings in hidrocystoma (HC) of the lip

Author [ref.]	Age	Sex	Number (localization) (size)	Clinical diagnosis	Pathological diagnosis	Immunohistochemistry								
						CK7	CK8	CK18	CK19	EMA	S100	α -SMA	Mamma-globin/ (HMFG)	GCDFP-15
De Viragh PA et al. [3]	73	F	Multiple (lip) (?)	HC, BCC	Eccrine HC	–	–	–	NA	NA	NA	–	–	NA
Willard K et al. [5]	65	F	Solitary (right upper lip) (2 mm)	HC, BCC	Eccrine HC ?	NA	NA	NA	NA	NA	NA	NA	NA	NA
Andersen WA et al. [6]	39	M	Solitary (right lip) (2 mm)	Cyst	Hybrid epidermoid and apocrine cyst	NA	NA	NA	NA	NA	NA	NA	NA	–
Our case	64	M	Solitary (right lower lip) (4 × 4 mm)	Tumor	Apocrine HC	+	+	+	+	+	+	+	+	+
						I-Cs	I-Cs	I-Cs	I-Cs	I-Cs	I-Cs	My-Cs	I-Cs	I-Cs
										B-Cs	B-Cs			

M mail, F female, HC hidrocystoma, BCC basal cell carcinoma, I-Cs inner cells, B-Cs basal cells, My-Cs myoepithelial cells, CK cytokeratin, EMA epithelial membrane antigen, α SMA alpha-smooth muscle actin, HMFG human milk fat globule, GCDFP-15 gross cystic disease fluid protein 15, + positive, – negative, NA not available, ? unknown

Here we report an extremely rare case of apocrine -HC on the lower lip, including its histological and immunohistochemical features, and discuss the differences between HCs and minor salivary gland cystic lesions.

Materials and Methods

Case Report

A 64-year-old Japanese man was referred to Hanyu General Hospital because of a pain-less mass (4 × 4 mm) in the right lower lip with normal coloration (Fig. 1). The clinical diagnosis was a suspected tumor, and the lesion was resected under local anesthesia. Macroscopically, the surgical specimen was a cystic lesion with a smooth surface (Fig. 2a). Microscopic examination showed that the lesion contained multilocular spaces (Fig. 2b). The cystic ducts were lined mainly by double -layered epithelium (Fig. 3), with no evidence of squamous or mucous metaplasia. Occasional ductal components showed diffusely apocrine-like secretory epithelium, and focal papillary epithelial hyperplasia without a vascular core (Fig. 3). Immunohistochemistry showed that the myoepithelial cells of the cystic wall were positive for α -SMA (Fig. 4a), and that the proliferative activity (MIB 1 index) of the cystic epithelium was low, at about <1 % (Fig. 4b). The apocrine-like secretory epithelium was positive for mammary-globin and GCDFP-15 (Fig. 4c, d). CK7, CK14 (data not shown), CK18 and CK19 were expressed in the luminal cell layer of the cystic lining epithelium (Fig. 4e–g). EMA

and S100 protein were expressed in the basal and luminal cell layers (data not show). Myoepithelial cells were weakly positive for S100 protein (data not show). These histological findings indicated that the lesion was compatible with apocrine -HC of the lower lip.

The case study protocol was reviewed and approved by the Research Ethics Committee of Meikai University School of Dentistry (A0832).

Immunohistochemistry

Deparaffinized sections were immersed in absolute methanol containing 0.3 % H₂O₂ for 15 min at room temperature to block endogenous peroxidase activity. After washing, the sections were immersed in 0.01 M citrate

Fig. 1 A swelling lesion with normal color in the right lower lip-skin (arrow)

Fig. 2 Surgical and microscopic features of the lesion. **a** A cystic lesion with capsule preserved in subepidermis. **b** The survey view of the resected specimen shows an encapsulated multi-loculated solid cyst and irregular cystic space with eosinophilic fluids (HE, original magnification $\times 12.5$)

buffer, pH 6.0, and heated in a microwave oven for 5 min at high voltage and then for 15 min at low voltage. They were then incubated with each of the appropriately diluted antibodies listed in Table 2. After washing, the sections were incubated with a pre-diluted anti-mouse or rabbit IgG antibody conjugated with peroxidase (Nichirei, Tokyo, Japan) for 30 min at room temperature. They were then immersed for 8 min in 0.05 % 3, 3'-diaminobenzidine tetrahydrochloride (DAB) in 0.05 M Tris-HCl buffer (pH 8.5) containing 0.01 % H_2O_2 , and counterstained with Mayer's hematoxylin for 90 s.

Discussion

Hidrocystomas are rare, benign skin adnexal cystic lesions [5]. On the basis of their histologic characteristics and presumed histogenic derivation, HCs have been

Fig. 3 Cyst wall covered by apocrine type epithelial cells with marked decapitation secretion “so-called” apocrine snout and fringe (arrowheads). Focally, papillary epithelial hyperplasia without vascular core was noted (HE, original magnification $\times 100$)

categorized into two types: apocrine- and eccrine -HCs. Apocrine -HC (apocrine cystadenoma), first described by Mehregan in 1964, is thought to be a benign skin cystic lesion derived from the secretory portion of the apocrine gland [1]. This lesion arises through proliferation of apocrine glands and is usually solitary, with a diameter of 3–15 mm [7, 8]. Apocrine lesions are also found mostly on the head and neck, and along the eyelid margin near the inner canthus [7]. Eccrine -HCs, first described by Robinson [9], present as small, tense, thin-walled cysts 1–6 mm in diameter, and can occur as single or multiple lesions [7, 8]. They occur predominantly in adult females, being located mostly in the periorbital and malar regions [7, 8]. Apocrine- and eccrine -HCs are prevalent in adults between 30 and 75 years of age, and the lesions are generally distributed in similar locations on the body [7, 8, 10, 11]. However, HCs in the lip-skin are very rare, and apocrine -HC of the lower lip is extremely rare (Table 1).

The most important pathological characteristics of apocrine- and eccrine -HCs are: (1) Clinically, solitary lesions are more likely to be apocrine -HCs than eccrine -HCs (multiple apocrine -HCs are found in Goltz-Gorlin syndrome and Schopf-Schulz-Passarge syndrome [12, 13]). (2) Morphologically, apocrine -HCs have a double lining of epithelium (inner layer, tall columnar or cuboidal cells) with decapitation secretion and an outer side consisting of myoepithelial cells, whereas eccrine -HCs are lined by flat epithelium without myoepithelial cells [3, 12]. (3) Immunohistochemically, apocrine -HCs are positive for human milk fat globules, GCDPF-15, CK7 and CK18 in the inner layer of epithelium, and also positive for α -SMA in the outer myoepithelial cells, whereas eccrine -HCs are negative for all of these [3, 4, 14, 15]. Therefore, the most

Fig. 4 Immunohistochemical features of the surgical specimen. **a** An outer layer of cystic wall was positive for α -SMA (arrowheads), **b** and proliferative activity (MIB 1 index) in the focal epithelial hyperplasia was low value (about < 1 %). **c, d** Apocrine-like secretory epithelium

and secretory fluids were strongly positive for mammaglobin and GCDFP-15. **e–g** The luminal cell layer of the lining epithelium was positive for CK7, CK18 and CK19. (**a–g**, original magnification $\times 100$)

Table 2 Antibodies and dilutions used in this case

Antigen	Clone	Dilution	Pretreatment	Source
Cytokeratin 7	OV-TL 12/30	1:50 (mouse monoclonal)	MW	Dako
Cytokeratin 14	LL002	1:50 (mouse monoclonal)	MW	Chemicon international
Cytokeratin 18	DC 10	1:50 (mouse monoclonal)	MW	Dako
Cytokeratin 19	RCK 108	1:50 (mouse monoclonal)	MW	Dako
S100 protein	–	1:400 (rabbit polyclonal)	–	Nichirei Biosciences
Ki-67	MIB-1	1:50 (mouse monoclonal)	MW	Dako
Epithelial membran antigen (EMA)	E29	1:1 (mouse monoclonal)	–	Nichirei Biosciences
Alpha-smooth muscle actin (α -SMA)	1A4	1:1 (mouse monoclonal)	–	Nichirei Biosciences
Mammaglobin	31A5	1:1 (rabbit polyclonal)	–	Biocare Medical
Gross cystic disease fluid protein 15 (GCDFP-15)	D6	1:1 (mouse monoclonal)	–	Biocare Medical

MW microwave oven (for 5 min at high voltage and then for 10 min at low voltage); –, non

compatible pathological diagnosis in the present case was apocrine -HC.

Pathological diagnosis of HCs in the lip is need differentiating from minor salivary gland cyst or cystic tumors. The differential diagnosis includes cystic pleomorphic adenoma (CPA), Warthin tumor (WT), cystadenoma (CA),

cystadenocarcinoma (CAC), mucoepidermoid carcinoma (MEC), salivary duct carcinoma (SDC), mucous retention cyst, salivary duct cyst, and sclerosing polycystic adenosis (SPA). Apocrine-HC lacks the myxoid to chondroid component and myoepithelial proliferation of CPA, and CPA lacks the apocrine-like secretory epithelium that

characterized apocrine -HC. Likewise, WT, CA, CAC, MEC, SDC, mucous retention cyst, and salivary duct cyst lacks this feature. The most important differentiating minor salivary gland lesion is SPA because it is histomorphologically very similar to apocrine -HC. SPA are characterized by apocrine-like epithelium (GCDFP-15 positive) [15], nodular sclerosis, xanthomatous infiltrate, acinar-type cells, and foamy degeneration of cyst-lining epithel cells, however, apocrine -HC essentially lacks nodular sclerosis “scar-like hyalinized fibrous stroma” and these feature except for apocrine-like epithelium (GCDFP-15 positive). Furthermore, in our case is found to be a cystic lesion rather than a tumor by low positive rate of ki-67. Clinically, the sweat gland lesion or minor salivary gland lesions are distinguishable by swelling side of the skin or oral mucosa. In the present case is swelling skin in the lip, and surgically operated lesion is presented in the subepidermis.

De Viragh et al. [3] have reported that apocrine- or eccrine -HCs are often misdiagnosed because of masking of the usual histological criteria, probably secondary to the intraluminal pressure in the cysts, which flattens their walls and abolishes decapitation secretion. Furthermore, the immunohistochemical staining for CK8 or 19 may not be consistent, varying among manufacturers even for the same antibody [14, 16]. Similarly, their differentiation cannot be confirmed by staining for carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA) [4], and the use of S100 protein immunostaining for differentiating eccrine from apocrine cystic tumors is controversial [17–20]. HCs may be eccrine or apocrine, and a specific diagnosis is possible only after staining for human milk fat globules or GCDFP-15 [3].

Although many of the cystic lesions occurring in the lip are a minor salivary gland origin, HC which originates in skin sweat gland rarely may arise. The available literature suggests that distinction of eccrine- from apocrine -HCs can be achieved by immunohistochemical staining for human milk fat globules, GCDFP-15 or mammaglobin.

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